

Claims

1. A method for quantitatively determining cholesterol in high-density lipoprotein, which comprises:

reacting a sample with cholesterol esterase and cholesterol oxidase or cholesterol esterase, an oxidized coenzyme and cholesterol dehydrogenase in an aqueous medium comprising a bile acid derivative; and

measuring the formed hydrogen peroxide or a reduced coenzyme.

2. The method according to claim 1, wherein the aqueous medium further comprises albumin.

3. The method according to claim 1 or 2, wherein the cholesterol esterase is chemically modified cholesterol esterase.

4. The method according to claim 3, wherein the chemically modified cholesterol esterase is cholesterol esterase which is modified by a group selected from the group consisting of a group having poly(ethylene glycol) as a main component, a group having poly(propylene glycol) as a main component, a group having a copolymer of poly(propylene glycol) and poly(ethylene glycol), a group having a water-soluble polysaccharide, a sulfopropyl group, a sulfobutyl group, a polyurethane group and a group having a chelating function.

5. The method according to claim 3, wherein the chemically

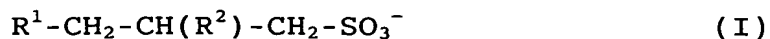
modified cholesterol esterase is cholesterol esterase which is modified by a group having poly(ethylene glycol) as a main component.

6. The method according to any one of claims 1 to 5, wherein the bile acid derivative is a bile acid derivative having an anionic surface activity.

7. The method according to claim 6, wherein the bile acid derivative having an anionic surface activity is selected from the group consisting of cholic acid or a salt thereof, taurocholic acid or a salt thereof, glycocholic acid or a salt thereof, lithocholic acid or a salt thereof, deoxycholic acid or a salt thereof, chenodeoxycholic acid or a salt thereof, ursodeoxycholic acid or a salt thereof, 7-oxolithocholic acid or a salt thereof, 12-oxolithocholic acid or a salt thereof, 12-oxochenodeoxycholic acid or a salt thereof, 7-oxodeoxycholic acid or a salt thereof, hyocholic acid or a salt thereof, hyodeoxycholic acid or a salt thereof and dehydrocholic acid or a salt thereof.

8. The method according to any one of claims 1 to 5, wherein the bile acid derivative is a bile acid derivative having an amphoteric surface activity.

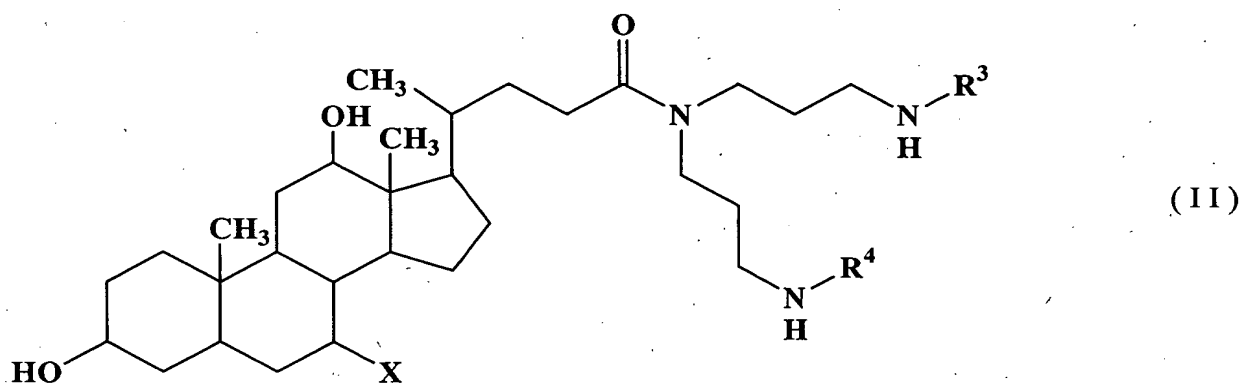
9. The method according to claim 8, wherein the bile acid derivative having an amphoteric surface activity is a compound represented by the formula (I)



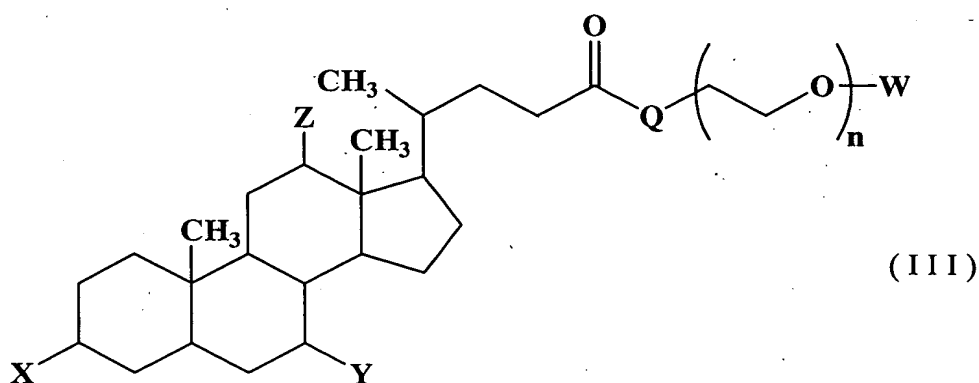
[wherein R^1 is a 3-(3-cholamidopropyl)dimethylammonio group and R^2 is a hydrogen atom or a hydroxyl group].

10. The method according to any one of claims 1 to 5, wherein the bile acid derivative is a bile acid derivative having a nonionic surface activity.

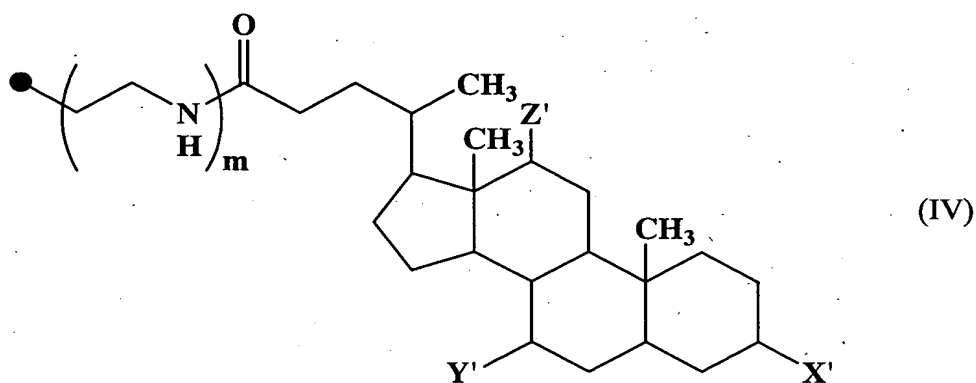
11. The method according to claim 10, wherein the bile acid derivative having a nonionic surface activity is a compound represented by the formula (II)



(wherein X is a hydrogen atom or a hydroxyl group; R^3 and R^4 may be the same or different and each represents a substituted or unsubstituted alkyl group or a substituted or unsubstituted alkanoyl group) or a compound represented by the formula (III)



{wherein X, Y and Z may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo (=O) group; Q is an oxygen atom or NH; W is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, a cycloalkenyl group, an alkanoyl group, an alkenoyl group, an alkynoyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aminoalkyl group or a group represented by the formula (IV)}



[wherein X', Y' and Z' may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo (=O) group; and m is 0 or 1]; and n is an integer of 3 to 400}.

12. A reagent for quantitatively determining cholesterol in high-density lipoprotein, which comprises cholesterol esterase, cholesterol oxidase, a bile acid derivative and a reagent for quantitatively determining hydrogen peroxide.

13. A reagent for quantitatively determining cholesterol in high-density lipoprotein, which comprises cholesterol esterase, cholesterol dehydrogenase, a bile acid derivative and

an oxidized coenzyme.

14. The reagent according to claim 13, which further comprises a reagent for quantitatively determining a reduced coenzyme.

15. The reagent according to any one of claims 12 to 14, which further comprises albumin.

16. The reagent according to any one of claims 12 to 15, wherein the cholesterol esterase is chemically modified cholesterol esterase.

17. The reagent according to claim 16, wherein the chemically modified cholesterol esterase is cholesterol esterase which is modified by a group selected from the group consisting of a group having poly(ethylene glycol) as a main component, a group having poly(propylene glycol) as a main component, a group having a copolymer of poly(propylene glycol) and poly(ethylene glycol), a group having a water-soluble polysaccharide, a sulfopropyl group, a sulfobutyl group, a polyurethane group and a group having a chelating function.

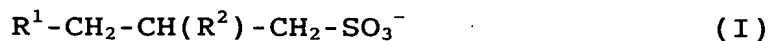
18. The reagent according to claim 16, wherein the chemically modified cholesterol esterase is cholesterol esterase which is modified by a group having poly(ethylene glycol) as a main component.

19. The reagent according to any one of claims 12 to 18, wherein the bile acid derivative is a bile acid derivative having an anionic surface activity.

20. The reagent according to claim 19, wherein the bile acid derivative having an anionic surface activity is selected from the group consisting of cholic acid or a salt thereof, taurocholic acid or a salt thereof, glycocholic acid or a salt thereof, lithocholic acid or a salt thereof, deoxycholic acid or a salt thereof, chenodeoxycholic acid or a salt thereof, ursodeoxycholic acid or a salt thereof, 7-oxolithocholic acid or a salt thereof, 12-oxolithocholic acid or a salt thereof, 12-oxochenodeoxycholic acid or a salt thereof, 7-oxodeoxycholic acid or a salt thereof, hyocholic acid or a salt thereof, hyodeoxycholic acid or a salt thereof and dehydrocholic acid or a salt thereof.

21. The reagent according to any one of claims 12 to 18, wherein the bile acid derivative is a bile acid derivative having an amphoteric surface activity.

22. The reagent according to claim 21, wherein the bile acid derivative having an amphoteric surface activity is a compound represented by the formula (I)

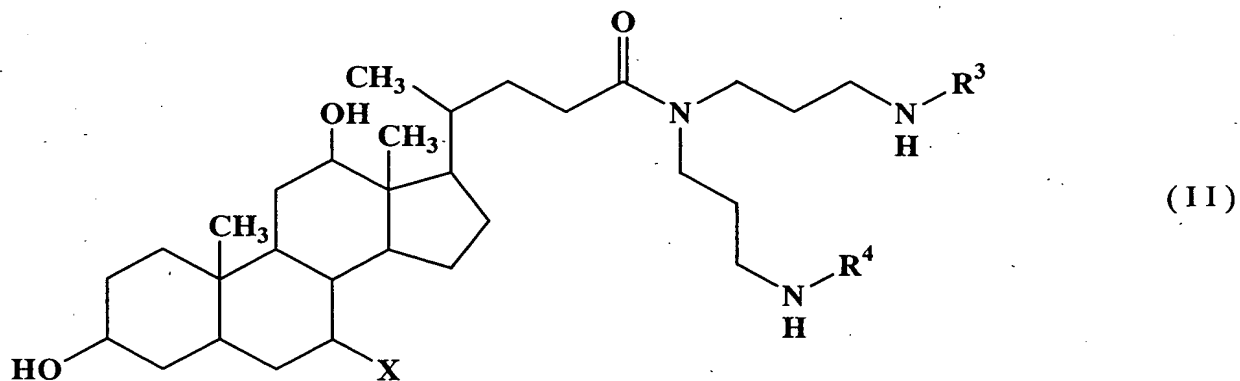


[wherein R^1 is a 3-(3-cholamidopropyl)dimethylammonio group and R^2 is a hydrogen atom or a hydroxyl group].

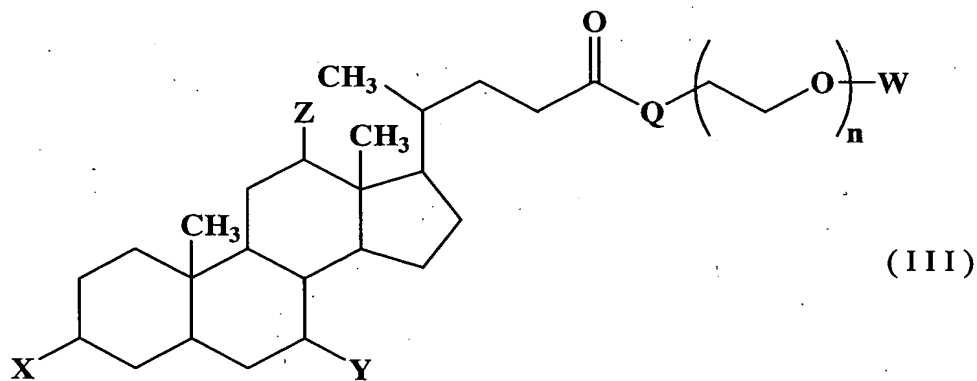
23. The reagent according to any one of claims 12 to 18, wherein the bile acid derivative is a bile acid derivative having a nonionic surface activity.

24. The reagent according to claim 23, wherein the bile

acid derivative having a nonionic surface activity is a compound represented by the formula (II)

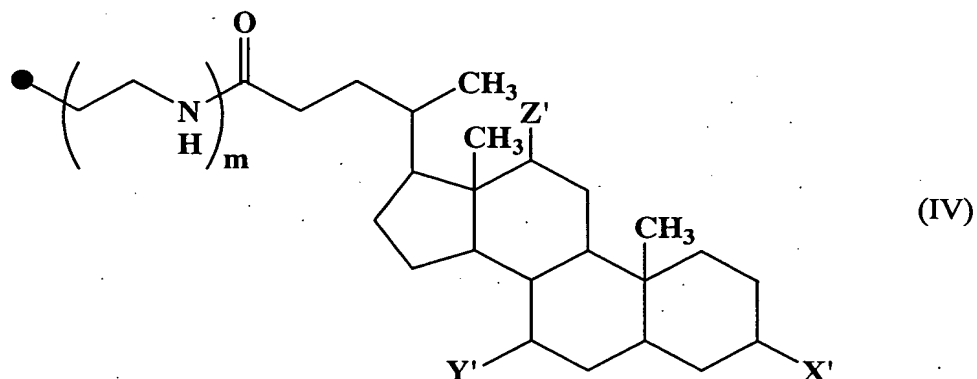


(wherein X is a hydrogen atom or a hydroxyl group; R³ and R⁴ may be the same or different and each represents a substituted or unsubstituted alkyl group or a substituted or unsubstituted alkanoyl group) or a compound represented by the formula (III)



{wherein X, Y and Z may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo (=O) group; Q is an oxygen atom or NH; W is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, a cycloalkenyl group, an alkanoyl group, an alkenoyl group, an alkynoyl group, a substituted or unsubstituted aryl group, a

substituted or unsubstituted aminoalkyl group or a group represented by the formula (IV)



[wherein X' , Y' and Z' may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo ($=\text{O}$) group; and m is 0 or 1]; and n is an integer of 3 to 400}.

25. A kit for quantitatively determining cholesterol in high-density lipoprotein, which comprises a first reagent comprising cholesterol esterase and a second reagent comprising cholesterol oxidase, wherein a bile acid derivative and a reagent for quantitatively determining hydrogen peroxide are comprised in either or both of the first reagent and/or the second reagent.

26. A kit for quantitatively determining cholesterol in high-density lipoprotein, which comprises a first reagent comprising a bile acid derivative and a second reagent comprising cholesterol esterase and cholesterol oxidase, wherein a reagent for quantitatively determining hydrogen peroxide is comprised in either or both of the first reagent and/or the second reagent.

27. A kit for quantitatively determining cholesterol in

high-density lipoprotein, which comprises a first reagent comprising a reagent for quantitatively determining hydrogen peroxide a second reagent comprising cholesterol esterase and cholesterol oxidase wherein a bile acid derivative is comprised in either or both of the first reagent and/or the second reagent.

28. A kit for quantitatively determining cholesterol in high-density lipoprotein, which comprises a first reagent cholesterol esterase and a second reagent comprising cholesterol dehydrogenase where a bile acid derivative and an oxidized coenzyme are comprised in either or both of the first reagent and/or the second reagent.

29. A kit for quantitatively determining cholesterol in high-density lipoprotein, which comprises a first reagent comprising a bile acid derivative and a second reagent comprising cholesterol esterase and cholesterol dehydrogenase wherein an oxidized coenzyme is comprised in either or both of the first reagent and/or the second reagent.

30. The kit according to claim 28 or 29, which further comprises a reagent for quantitatively determining a reduced coenzyme in either or both of the first reagent and/or the second reagent.

31. The kit according to any one of claims 25 to 30, which further comprises albumin in either or both of the first reagent and/or the second reagent.

32. The kit according to any one of claims 25 to 31, wherein

the cholesterol esterase is chemically modified cholesterol esterase.

33. The kit according to claim 32, wherein the chemically modified cholesterol esterase is cholesterol esterase which is modified by a group selected from the group consisting of a group having poly(ethylene glycol) as a main component, a group having poly(propylene glycol) as a main component, a group having a copolymer of poly(propylene glycol) and poly(ethylene glycol), a group having a water-soluble polysaccharide, a sulfopropyl group, a sulfobutyl group, a polyurethane group and a group having a chelating function.

34. The kit according to claim 32, wherein the chemically modified cholesterol esterase is cholesterol esterase which is modified by a group having poly(ethylene glycol) as a main component.

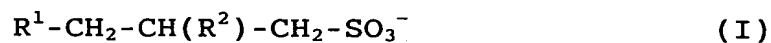
35. The kit according to any one of claims 25 to 34, wherein the bile acid derivative is a bile acid derivative having an anionic surface activity.

36. The kit according to claim 35, wherein the bile acid derivative having an anionic surface activity is selected from the group consisting of cholic acid or a salt thereof, taurocholic acid or a salt thereof, glycocholic acid or a salt thereof, lithocholic acid or a salt thereof, deoxycholic acid or a salt thereof, chenodeoxycholic acid or a salt thereof, ursodeoxycholic acid or a salt thereof, 7-oxolithocholic acid

or a salt thereof, 12-oxolithocholic acid or a salt thereof, 12-oxochenodeoxycholic acid or a salt thereof, 7-oxodeoxycholic acid or a salt thereof, hyocholic acid or a salt thereof, hyodeoxycholic acid or a salt thereof and dehydrocholic acid or a salt thereof.

37. The kit according to any one of claims 25 to 34, wherein the bile acid derivative is a bile acid derivative having an amphoteric surface activity.

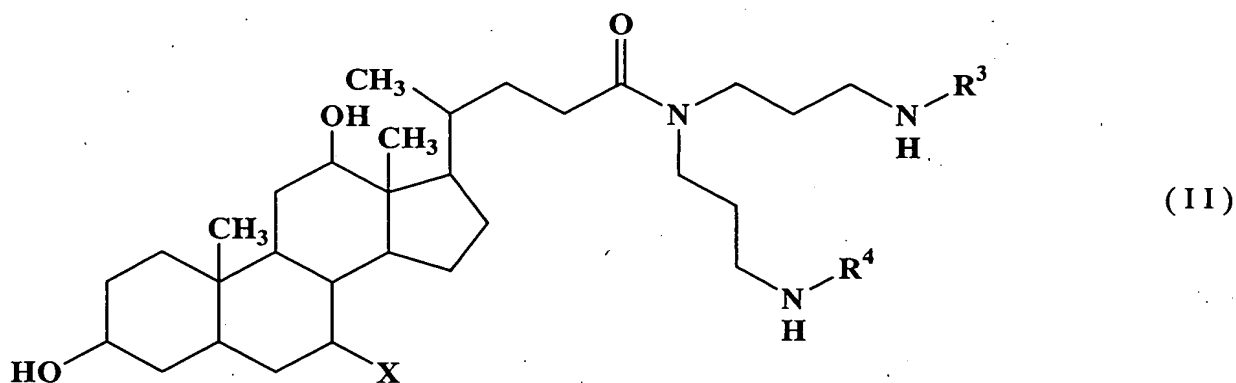
38. The kit according to claim 37, wherein the bile acid derivative having an amphoteric surface activity is a compound represented by the formula (I)



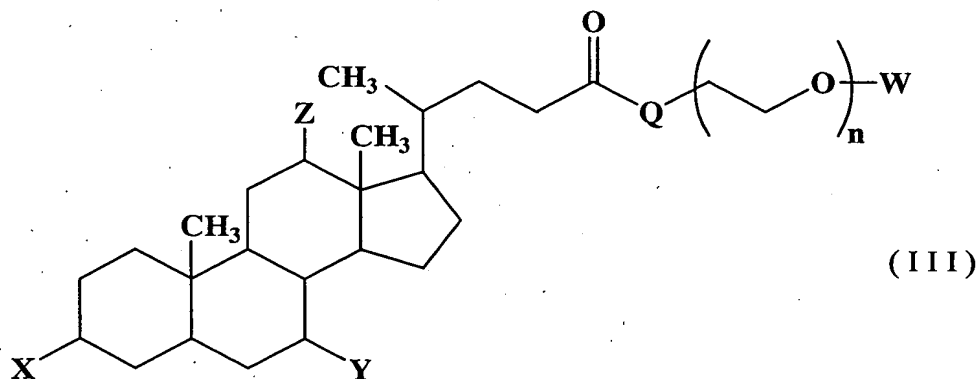
[wherein R^1 is a 3-(3-cholamidopropyl)dimethylammonio group and R^2 is a hydrogen atom or a hydroxyl group].

39. The kit according to any one of claims 25 to 34, wherein the bile acid derivative is a bile acid derivative having a nonionic surface activity.

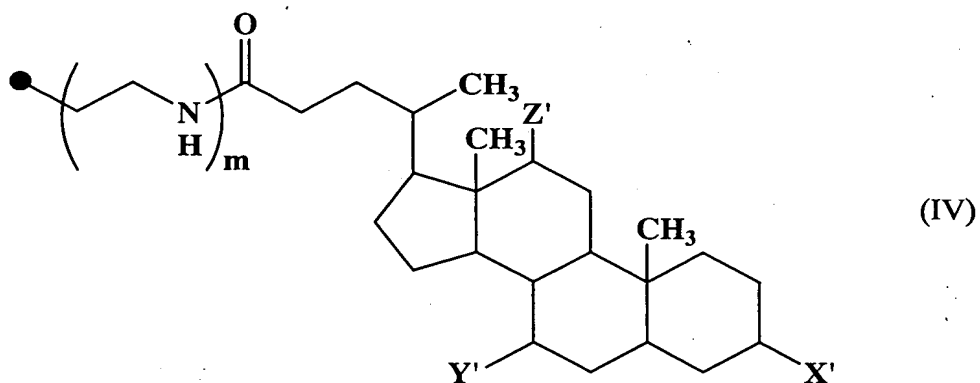
40. The kit according to claim 39, wherein the bile acid derivative having a nonionic surface activity is a compound represented by the formula (II)



(wherein X is a hydrogen atom or a hydroxyl group; R³ and R⁴ may be the same or different and each represents a substituted or unsubstituted alkyl group or a substituted or unsubstituted alkanoyl group) or a compound represented by the formula (III)

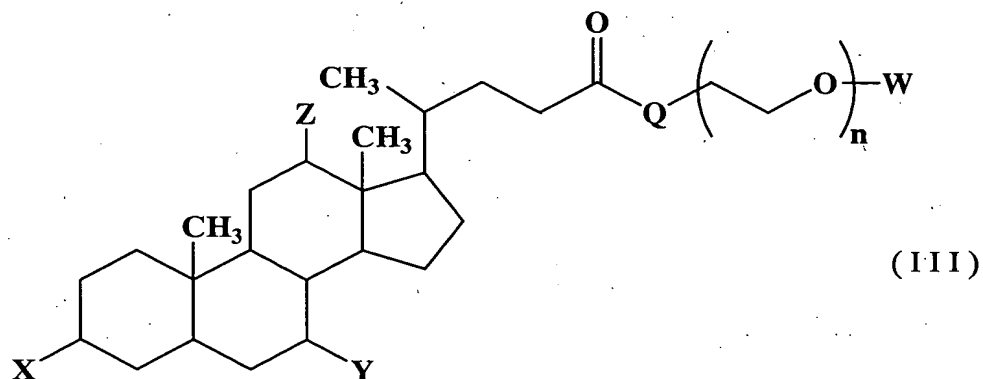


{wherein X, Y and Z may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo (=O) group; Q is an oxygen atom or NH; W is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, a cycloalkenyl group, an alkanoyl group, an alkenoyl group, an alkynoyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aminoalkyl group or a group represented by the formula (IV)}

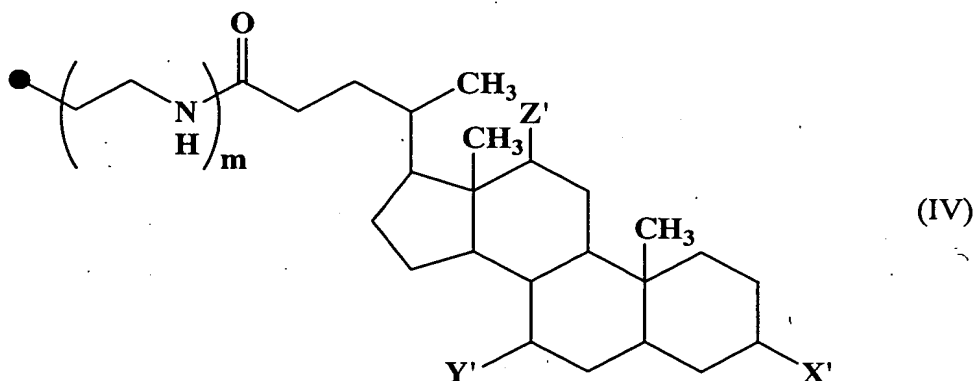


[wherein X' , Y' and Z' may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo ($=O$) group; and m is 0 or 1]; and n is an integer of 3 to 400}.

41. A compound represented by the formula (III)

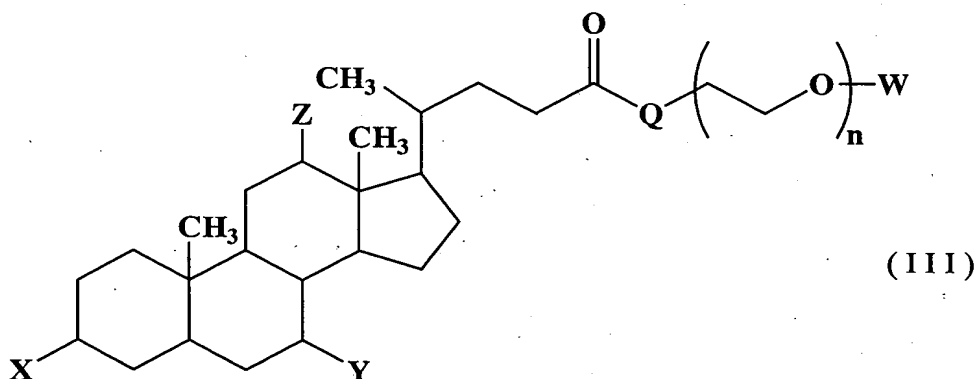


{wherein X , Y and Z may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo ($=O$) group; Q is an oxygen atom or NH ; W is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, a cycloalkenyl group, an alkanoyl group, an alkenoyl group, an alkynoyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aminoalkyl group or a group represented by the formula (IV)}



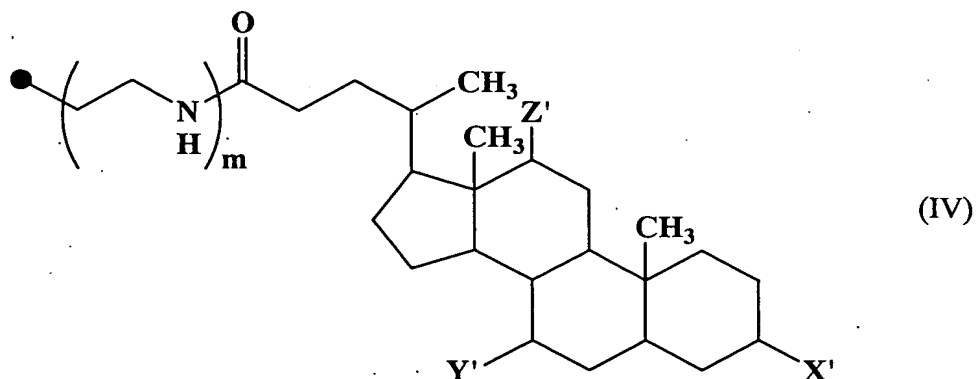
[wherein X', Y' and Z' may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo (=O) group; and m is 0 or 1]; and n is an integer of 3 to 400}.

42. A process for producing a compound represented by the formula (III)

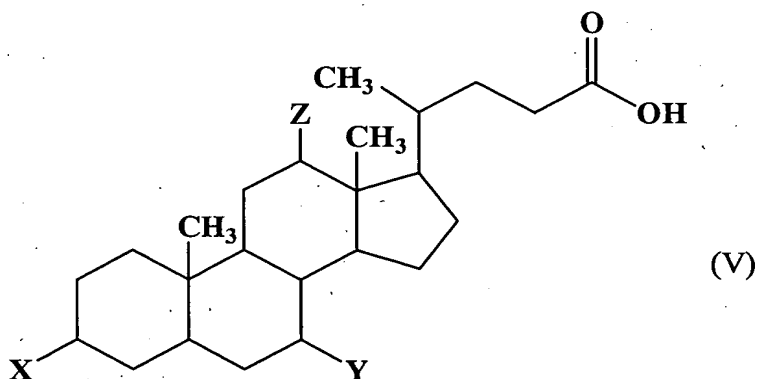


{wherein X, Y and Z may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo (=O) group; Q is an oxygen atom or NH; W is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, a cycloalkenyl group, an alkanoyl group, an alkenoyl group, an alkynoyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted aminoalkyl group or a group

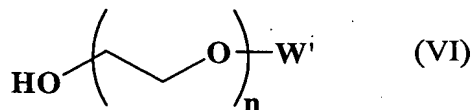
represented by the formula (IV)



[wherein X' , Y' and Z' may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo ($=O$) group; and m is 0 or 1]; and n is an integer of 3 to 400}, which comprises: reacting a compound represented by the formula (V)

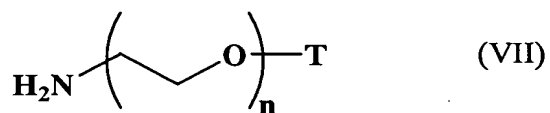


[wherein X , Y and Z may be the same or different and each represents a hydrogen atom, a hydroxyl group or an oxo ($=O$) group] with a compound represented by the formula (VI)



(wherein W' is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group, a cycloalkyl group, a cycloalkenyl group, an

alkanoyl group, an alkenoyl group, an alkynoyl group or a substituted or unsubstituted aryl group; and n is an integer of 3 to 400) or with a compound represented by the formula (VII)



(wherein T is a substituted or unsubstituted aminoalkyl group; and n is an integer of 3 to 400) in the presence of a condensing agent.